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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,361	10/31/2003	Czeslaw Radziejewski	REG 930A	3038

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EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,361	RADZIEJEWSKI ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-20 and 22-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-20 and 22-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 16 December 2004 is acknowledged and has been entered. Specifically, it has been acknowledged that Applicants affirmed the election without traverse of Group II and claims 1-16 have been cancelled.

Claim Objections

2. Claim 17 is objected to because of the following informalities: step (c) recites the limitation "exposing each treated biosensor surface to a each mAb" in lines 6-7 of the instant claim. The phrase "to a each mAb" in the limitation seems to have an extra term that does not belong in the phrase or is missing terms. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 17-20 and 22-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. In claims 17 (lines 1-2), 25 (line 1), and 28 (line 1), the term "sibling monoclonal antibodies" is vague and indefinite. The specification does not provide a definition for the term and it is unclear as to what types of monoclonal antibodies are claimed. How does the term "sibling" limit the monoclonal antibodies in the instant term?

6. In claims 23 and 34, lines 1-2, the phrase "the agent is an enzyme and a chemical agent" is vague and confusing. The specification does not define the term "agent" and it is unclear as to how an agent can be both an enzyme and a chemical at the same time. Page 6, section 0029, lines 1-3 of the specification discloses that "modification or alteration of macromolecule structure is effected by either chemical treatment that tends to modify side chains of particular amino acid residues of the antigen protein, or by enzymatic treatment". The specification does not provide disclosure of how modification can be performed by an agent that is both an enzyme and a chemical agent. If it is Applicant's intention that any enzyme can be labeled as a chemical and vice versa, then prior art teaching an enzyme agent, but not specifically a chemical agent, or prior art teaching a chemical agent, but not specifically an enzyme, can be applied towards the instant claim.

7. Claims 17, 25, and 28 recite the limitation "the antigen" in line 3 of the claims. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 17-19, 23-26, 28-32, and 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Colyer et al (WO 00/50902) in view of Fagerstam et al (Journal of Molecular Recognition, 1990, vol. 3, no. 5/6, pp. 208-214).

In the instant claims, Colyer et al reference teaches one or more immobilized polypeptides on a support (i.e. immobilizing the antigen on a biosensor surface), contacting the immobilized polypeptide with a test sample which may contain an agent capable of modifying the immobilized polypeptide (i.e. treating the biosensor surface with an agent, wherein each agent is capable of modifying a surface of the immobilized antigen), contacting the immobilized polypeptide with a binding partner polypeptide, wherein the binding of this partner polypeptide to the immobilized polypeptide is at least partly dependent on the modification state of the immobilized polypeptide (i.e. exposing the treated biosensor surface to a binding partner), and measuring the association of the binding partner polypeptide to the immobilized polypeptide (i.e. determining a binding profile for the binding partner). See page 6, lines 14-24. In addition, Colyer et al reference teaches that peptide sequences, each containing at least a single modification site for a different enzyme are immobilized at discrete locations on a physical support (i.e. at least two biosensor surfaces; treating each biosensor surface with a different agent). See page 20, lines 21-27.

However, Colyer et al reference fails to teach that the binding partner is a mAb, wherein there are multiple mAbs, and also fails to teach the step of classifying the mAbs into functional groups based on the binding profiles, wherein mAbs that exhibit similar

binding profiles to each treated sensor surface are classified into the same functional group.

Fagerstam et al reference teaches the step of testing all possible pairs of MoAbs in a double antibody binding assay by exposing the MoAbs to immobilized HIV-1 core protein p24 on a sensor chip (i.e. multiple Abs exposed to each biosensor surface), wherein MoAbs showing the same pattern are assigned to the same epitope (i.e. classifying the mAbs into functional groups based on the binding profiles), in order to perform epitope mapping in early screening procedures and elucidate the binding pattern of MoAbs. See page 208, right column, 2nd paragraph, lines 1-6; page 209, left column, 2nd paragraph and last paragraph to right column, 1st paragraph; page 213, right column, 3rd paragraph, lines 7-9; and Figure 5 and Table 1.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Colyer et al with the step of testing all possible pairs of MoAbs in a double antibody binding assay by exposing the MoAbs to immobilized HIV-1 core protein p24 on a sensor chip (i.e. multiple Abs exposed to each biosensor surface), wherein MoAbs showing the same pattern are assigned to the same epitope (i.e. classifying the mAbs into functional groups based on the binding profiles), as taught by Fagerstam et al, in order to perform epitope mapping in early screening procedures and elucidate the binding pattern of MoAbs. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in testing all possible pairs of MoAbs in double antibody binding assays and assigning MoAbs showing the same pattern to the same epitope, as taught by Fagerstam et al, in the method of

Colyer et al, since Colyer et al reference teaches specific binding between a free and immobilized molecule, and the step taught by Fagerstam et al involve free MoAb binding to immobilized p24 antigen. In addition, Colyer et al reference teaches binding between immobilized polypeptides and a binding partner, and Fagerstam et al reference teaches that MoAbs can also act as binding partners to polypeptides by disclosing that free MoAbs can bind to synthetic p24 peptides, which are types of polypeptides. See page 209, right column 3rd paragraph.

Specifically with regards to the limitation wherein "each mAb is exposed to each treated biosensor surface" (lines 6-7 of claim 17), Colyer et al reference teaches that each discrete location of immobilized polypeptides is modified by a different enzyme, and that partner polypeptides bind to each of the locations, as stated above, which anticipates the part of the limitation that states "exposed to each treated biosensor surface". The missing part of the limitation of "each mAb is exposed" is anticipated by Fagerstam et al reference with the teaching that at least two monoclonal antibodies are contact with an immobilized p24 peptide, as stated above.

With regards to claims 18-19, 23-26, 28-29, 31-32, and 34-35, Colyer et al reference teaches that modifications can include proteolysis and are performed by enzymes (i.e. proteolytic enzyme), wherein the enzyme can be chymotrypsin (i.e. trypsin and chymotrypsin). See page 8, line 30 to page 9, line 8; page 19, lines 29-30; and page 60, lines 20-26.

With regards to claim 30, Fagerstam et al reference teaches that the MoAb are in hybridoma supernatant (i.e. supernatant from a mAb-containing clone culture). See

page 209, left column, 2nd paragraph, lines 1-4, and last paragraph to right column, 2nd paragraph.

12. Claims 20 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Colyer et al (WO 00/50902) in view of Fagerstam et al (Journal of Molecular Recognition, 1990, vol. 3, no. 5/6, pp. 208-214), as applied to claims 17 and 30 above, and further in view of Lin et al (Journal of Food Science, 1976, vol. 41, no. 5, pp. 1056-1060).

Colyer et al and Fagerstam et al references have been disclosed above, and Colyer et al reference additionally teaches that chemical agents may modify the polypeptide (i.e. chemical agents). See page 9, lines 8-9. However, Colyer et al and Fagerstam et al references fail to teach that the chemical agent is glutaraldehyde.

Lin et al reference teaches chemical modification of a collagen membrane by glutaraldehyde to cross-link the collagen membrane, in order to determine the effect of the chemical modification on the binding capacity of the collagen membrane. See page 1057, left column, 6th paragraph, lines 1-3 and 11th paragraph, lines 1-4.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Colyer et al and Pfund et al, with chemical modification of a collagen membrane by glutaraldehyde to cross-link the collagen membrane, as taught by Lin et al, in order to determine the effect of the chemical modification on the binding capacity of the collagen membrane. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in

using glutaraldehyde to modify the structure of collagen, as taught by Lin et al, in the method of Colyer et al and Fagerstam et al, since Colyer et al and Fagerstam et al teach the modification of polypeptides using chemicals, and glutaraldehyde is one example of a chemical that can alter the structural conformation of proteins.

13. Claims 22, 27, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Colyer et al (WO 00/50902) in view of Fagerstam et al (Journal of Molecular Recognition, 1990, vol. 3, no. 5/6, pp. 208-214) as applied to claims 17 and 30 above, and further in view of Otterness et al (US 6,030,792).

Colyer et al and Fagerstam et al references have been disclosed above, and Fagerstam et al reference additionally teaches that the p24 peptides are immobilized on a BIAcore sensor chip. See page 209, left column, 1st paragraph. However, Colyer et al and Fagerstam et al references fail to teach that the at least two biosensor surfaces are four surfaces.

Otterness et al reference teaches four channels (i.e. four surfaces) of a BIAcore sensor, in order to couple a different protein to each of the channels and characterize binding of a monoclonal antibody to four different types of proteins. See column 13, line 62 to column 14, line 17.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Colyer et al and Fagerstam et al with four channels (i.e. four surfaces) of a BIAcore sensor, as taught by Otterness et al, in order to couple a different protein to each of the channels and characterize binding of a monoclonal

antibody to four different types of proteins. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including four channels, as taught by Otterness et al, in the method of Colyer et al and Fagerstam et al, since Colyer et al and Fagerstam et al teach a BIAcore sensor, and the four channels taught by Otterness et al are also in a BIAcore sensor. In addition, Colyer et al and Fagerstam et al teach monoclonal antibody binding to immobilized antigen, and the four channels of Otterness et al have immobilized antigen that also bind to a monoclonal antibody.

Response to Arguments

14. Applicant's arguments with respect to claims 17 and 20 have been considered but are moot in view of the new ground(s) of rejection.

Specifically, Applicant's amendment of independent claim 17 and addition of new independent claims 25, 28, and 30 recite the limitation of exposing each treated biosensor surface to "each mAb" in step (c), which alters the scope of the original claims and necessitate the new grounds of rejection.

15. Although new grounds of rejection has been applied, Colyer et al reference (WO 00/50902) has been maintained as the primary reference.

With respect to claim 17, Applicant argues on pages 7-8 of the Remarks that Colyer et al reference "do not describe or suggest (1) a method of classifying sibling

monoclonal antibodies into functional groups; (2) immobilizing the antigen onto at least two biosensor surfaces; (3) treating each biosensor surface with a different modifying agent; and (4) classifying the mAbs into functional groups based on the binding profiles, wherein mAbs that exhibit similar binding profiles to each treated sensor surface area classified into the same functional group." However, as stated above, Colyer et al reference is applied to teach steps (2) and (3), while Fagerstam et al reference (Journal of Molecular Recognition, 1990, vol. 3, no. 5/6, pp. 208-214) is applied to teach steps (1) and (4) with the motivation of performing epitope mapping in early screening procedures and the elucidate the binding pattern of MoAbs. Specifially, Colyer et al reference teaches peptide sequences immobilized at discrete locations of a physical support. See page 20, lines 21-27. Each physical location is considered to be separate embodiments and reads on step (2) with the limitation of "at least two biosensor surfaces". In addition, Colyer et al reference teaches that each peptide sequence in discrete locations are modified by a different enzyme. See page 20, lines 21-27. Since each discrete location is considered to be a different biosensor, and each location is modified by a different enzyme, the cited text reads on step (3) with the limitation of "treating each biosensor surface with a different modifying agent".

With respect to claim 20, Applicant on page 10 argues that Lin et al reference (Journal of Food Science, 1976, 41(5):1056-1060) "does not disclose, teach, or suggest (1) a method of classifying sibling monoclonal antibodies into functional groups; (2) immobilizing the antigen onto at least two biosensor surfaces; (3) treating each biosensor surface with a different modifying agent; and (4) classifying the mAbs into

functional groups based on the binding profiles, wherein mAbs that exhibit similar binding profiles to each treated sensor surface area classified into the same functional group." However, Lin et al reference is not applied to teach steps (1)-(4), which is claimed in claim 17, but to teach the specific limitation claimed in claim 20 of glutaraldehyde, as stated in the 35 USC 103(a) rejection supra. Colyer et al and Fagerstam et al references have already been applied in combination to teach steps (1)-(4) of claim 17, also stated in the 35 USC 103(a) rejection supra.

Conclusion

16. No claims are allowed.

17. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure:

Malmqvist et al (US 5,554,541) teach epitope mapping of monoclonal antibodies on surface plasmon resonance surfaces.

Collen (US 5,695,754) teach epitope mapping of a panel of 17 monoclonal antibodies raised against wild-type staphylkinase using a BIAcore instrument.

De La Lastra et al (Immunology, 1999, vol. 96, pp. 663-670) teach epitope mapping using surface plasmon resonance technology.

Rich et al (Current Opinions in Biotechnology, 2000, vol. 11, pp. 54-61) teach epitope mapping using surface plasmon biosensors.

Van Regenmortel et al (Journal of Molecular Recognition, 1998, vol. 11, pp. 163-167) teach functional mapping of binding sites using biosensors.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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